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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,065	09/24/2003	David M. Markovitz	UM-08388	5111

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EXAMINER	
COOK, LISA V	
ART UNIT	**PAPER NUMBER**
1641	

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12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/670,065	MARKOVITZ ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,20,21 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,20,21 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's election without traverse of Group II (claims 13-23) in the reply filed on 7/17/06 is reiterated. Claims 1-12, 15-19 and 22-23 have been canceled without prejudice or disclaimer. New claims 24-26 have been added. Currently claims 13-14, 20-21, and 24-26 are pending and under consideration.

2. Rejections and/or objections of record not restated herein have been withdrawn.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

4. The information disclosure statement filed October 5, 2007 has been considered as to the merits.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Sequence Non-Compliance

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132. Sequence identification numbers have been added to Table I on page 84 of the disclosure, however SEQ ID NO:8 it not in compliance because the specification recites that this sequence refers to amino acids 425 to 439. See page 5 of the response filed 10/5/07. This is not consistent with the sequence listing submitted 11/24/06 and the CRFE entered 11/29/06. It is suggested that the specification is corrected to indicate that SEQ ID NO:8 "refers to amino acids 425 to **440**".

Applicant is given THREE MONTHS from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 13 and dependent claims 14, 20-21 and 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 13 is directed to a method for pathogen killing in a subject. The method steps (a-b) merely recite a subject, a pathogen, and the administration of anti-vimentin antibody. However, the relationship of the pathogen and the subject is not known. This makes that claims vague and indefinite. It is not clear if the pathogen in present within the subject prior to antibody administration, if Applicant intends to administer a pathogen to the subject, or if the pathogen is apart of the claimed method. It is suggested that the relationship of the pathogen in the claimed method be clearly set forth in order to obviate this rejection. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 13-14, 20-21, and 24-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically the claims are drawn to a method of administering an anti-vimentin antibody to any and all subjects to treat a bacterial pathogen. This reads on *in vivo* vaccine procedures and the disclosure does not have support for this type of protocol. The specification teaches that anti-vimentin IgG antibodies may have a phagocytic and killing activity on MDM cells cultured *in vitro*. See page 72 lines 13-24 and example 4 on page 77, for example. The specification also exemplifies reduced *E.coli* septicemia and mortality. However, this reduction appears to be seen if anti-vimentin antibodies are administered 15 min prior to an *E. coli* injection. See examples 6 and 7 on pages 78-79. These teachings do not enable one skilled in the art to effectively practice a method for pathogen killing in a subject as set forth in the instant claims.

The prior art teaches that the presence of anti vimentin antibodies is linked to detrimental results in patients. See the abstract to Danskine et al. (Human Immunology, 2002, Vol.63, Supplement 1, pp S30) wherein anti-vimentin antibodies were correlated with acute and chronic cardiac transplantation rejection. Also see the reference to Yang et al. (Clinical and Experimental Immunology, April 2002, Vol.128, No.1, pp 169-174) were high levels of antivimentin antibodies are linked to IPF (idiopathic pulmonary fibrosis), NSIP (non-specific interstitial pneumonia), systemic lupus erythematosus, progressive systemic sclerosis and RA. Thus from the prior art teaching the administration of anti-vimentin antibodies to a subject would appear to induce diseases and/or disorders linked to bacterial pathogens. This is contrary to the instant invention which is directed to pathogen killing. See abstract and page 128 – Discussion.

Further, the specification does not set forth any *in vivo* data showing the protective ability of anti-vimentin antibody administration to a subject. Example 7 on page 79 teaches that "mice receiving goat anti-vimentin show a 38% reduction in mortality compared to those receiving *anti-vimentin antibody* free serum (figure 9)". However, this is only exemplified in 13 week old mice with lethal dosages of *E. coli* (J-96) wherein the mice were injected with goat anti-vimentin serum 15 min prior to *E. coli* (J-96) injection.. These particulars are not recited in the instant claims. Also, the specification does not demonstrate that this 38% reduction in mortality is due to pathogen killing. The reduction in mortality may be linked to parameters other than pathogen killing.

Therefore the broad claim of killing any and all bacterial pathogens, in any and all subjects, with any and all anti-vimentin antibodies is not enabled. The prior art teaches that species specific antibodies against vimentin have different reactivity. See abstract to Bohn et al. (Experimental Cell Research, Vol.201, No.1, July 1992, pages 1-7). The art also teaches that in vitro results can not predict in vivo antibody responses. See Pallini et al. (Journal of Neuro-Oncology, Vol. 49, 2000, pages 9-17).

As such the killing of a pathogen via the administration of anti-vimentin antibodies is not apparent and would require undue experimentation.

Devoid of results supporting in vivo killing of a pathogen by anti-vimentin antibodies, the skilled artisan would not be able to predict the outcome of the administration of the claimed anti-vimentin antibodies activity, i.e. would not be able to accurately predict if anti-vimentin antibodies agents would be useful in the claimed purpose.

The agents/drug/antibody/vaccine (having anti-vimentin antibody activity) art is highly unpredictable and the instant specification fails to provide any information that any one of the recited conjugates would provide immunity to a human from a bacterial pathogen. There are no immunological experiments provided to demonstrate that the claimed proteins or fragments are capable of mounting an efficient immune response and, more importantly, there are no challenge experiments to demonstrate that a person immunized with any one of the claimed anti-vimentin antibodies would be protected. There are no protocols provided which demonstrate which anti-*vimentin antibody* agents would be effective in immunization, nor are there any protocols detailing the amount of protein which is needed to mount a sufficient immune response. There is no teaching as to what would be the most effective route of administration for the claimed agents/drug/antibody/vaccine. There is merely a general outline of agents/drug/antibody/vaccine and their administration, which does not directly apply to the instant invention. It is unclear that one of skill in the art could follow these general guidelines and achieve immunization (protection/treatment) of a human against a pathogen without undue experimentation.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from in vitro antibody reactivity studies is problematic. Unfortunately, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit *in vivo* protective immunity. See Blasi et al. (Clinical Pulmonary Medicine, 2002, 9/1, 6-12 -Abstract) wherein *in vitro* data regarding *C. pneumonia* activity/treatment could not predict optimal dosing and length for in vivo activity/treatment.

Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful anti-*vimentin antibody* agent with out prior demonstration of efficacy in the particular diseases.

Specifically, anti-*vimentin antibodies* do not necessarily end up providing any protective immunoprotection and have actually been linked to various disease states. Yang et al. (Clinical and Experimental Immunology, April 2002, Vol.128, No.1, pp 169-174)

It has been set forth above that 1) the experimentation required to generate an agent/drug/antibody/vaccine which provides treatment in a mammal/human against *a pathogen* would be great as 2) there are no immunological experiments provided to demonstrate that the claimed agents are capable of mounting an efficient immune response and, more importantly, there are no challenge experiments to demonstrate that a person immunized with any one of the claimed anti-vimentin antibody agents would be protected from *a pathogen.*

There are no protocols provided which demonstrate which proteins or portions of the proteins would be effective in immunization, nor are there any protocols detailing the amount of protein which is needed to mount a sufficient immune response, 3) there are not working examples provided in the instant specification, 4) the nature of the invention is a method for producing an anti-vimentin antibody agents which would provide complete protection in a host against *a pathogen*, 5) the relevant skill of those in the art is high yet 6) the state of the prior art has been shown to be highly unpredictable as evidenced by the cited references and lastly 7) the claims broadly encompass agents which would provide protection in humans to any *pathogen.*

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue.

8. For reasons aforementioned, no claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The Group 1641 – Central Fax number is (571) 273-8300.

In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA or CANADA) or 571-272-1000.

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